

PATERNALLY INHERITED CHROMOSOMAL DEFECTS ASSESSED IN MOUSE TWO-CELL EMBRYO METAPHASES USING MULTICOLOR FISH PAINTING

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We have applied multicolor FISH painting to the analysis of mouse two-cell (2-Cl) embryo metaphases. This method allows us to detect cytogenetic defects that are associated with three types of pregnancies outcomes: pregnancy loss (complex rearrangements, dicentrics), birth defects (reciprocal translocations) and mosaicism (numerical and structural). We determined the baseline frequencies of these defects in untreated mice. Over 508 2-Cl embryos were prepared from mating of B6C3F1 parents, and were hybridized with a DNA mixture containing 4 biotin-labeled painting probes specific for chromosomes 1, 2, 3 and X, plus a digoxigenin-labeled probe for chromosome Y. Out of 94 2-Cl embryos analyzed 7.5% were cytogenetically abnormal: 3 hypodiploid (each metaphase had 39 chrs); 1 numerical mosaic (one metaphase had 36 chrs including 2 Y chrs; the other metaphase had 44 chrs and no Y chromosome); 1 structural mosaic (one metaphase showed a chromatid deletion); and 2 triploids. One of the triploid embryos was due to dispermic fertilization as revealed by the presence of two Y chromosomes in each metaphase. There were also two asynchronous embryos in which one blastomere was at metaphase while the other was still in interphase. To characterize chromosomal damage induced in postmeiotic male germ cells on 2-Cl embryos, male mice were treated with 5 daily injections of 50 mg/kg of acrylamide and bred with untreated females at times that corresponded to fertilization with treated sperm or spermatids. The comparison of cytogenetic defects in 2-Cl metaphases with data already obtained for 1-Cl metaphases (Marchetti et al., 1996, Environ.Mol. Mutagen., 27, suppl. 27:44) will provide important information on the developmental consequences of specific chromosomal damage transmitted via paternal germ cells. (Work performed under the auspices of the U.S. DOE by the Lawrence Livermore National Laboratory under contract W-7405-ENG-48 with support from NIEHS Y01-ES-10203-00).